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"DEVELOPMENT AND TESTING OF A MOUSE SIMULATED SPACE FLIGHT MODEL"

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INTRODUCTION

We have recently completed this project concerning the development and testing of a mouse model for simulating some aspects of weightlessness that occurs during space flight, and the carrying out of immunological experiments on animals undergoing space flight. The mouse model we have developed was an antiorthostatic, hypokinetic, hypodynamic suspension model similar to the one used with rats [1-3].

Our subsequent studies were divided into two parts. The first involved determination of which immunological parameters should be observed on animals flown during space flight or studied in the suspension model. The second involved suspending mice and determining which of those immunological parameters were altered by the suspension. In addition, we were fortunate to be able to test our hypotheses using rats that were actually flown in Space Shuttle SL-3.

We believe the studies carried out during this project were highly successful. They have yielded much insight to allow for planning of future immunological experiments for space flight in the Space Shuttle and, possibly, for Space Station.

METHODS, RESULTS AND DISCUSSION

Our first studies involved the development of a murine antiorthostatic suspension model [3]. This model was similar to the model developed for rats [1,2]. Similar effects of antiorthostatic suspension on muscle, bone, electrolyte levels and urine and feces output were observed using the mouse model as were observed using the established rat model [3].

We next began studies to determine which immunological parameters were most important to study. We chose interferons because of their significant activities as immunoregulators [4]. We were able to show that interferons could affect the course of a wide variety of infections, including protozoan [5-9] and bacterial [10-12] infections. Therefore, we established that interferons played a major role in regulating resistance to a wide variety of infections, and were worthy of study in animals exposed to space flight.

Our next phase of work was to use the mouse antiorthostatic suspension model to determine its effects on interferon production. Mice suspended for one or two weeks in the model showed inhibited interferon production [13]. The inhibition of interferon induction was transient, as suspended mice returned to normal caging for one week had restored interferon production. Orthostatically suspended control mice had normal interferon production, suggesting that more than just the stress of suspension was responsible for the inhibition of interferon induction observed in antiorthostatically suspended mice [13].

Additional studies were carried out to determine how antiorthostatic suspension affected resistance to an infection. Female Swiss mice are normally completely resistant to infection with the D variant of

encephalomyocarditis virus (EMC-D virus) [14]. Mice that were suspended antiorthostatically became susceptible to infection [14], while orthostatically suspended control mice remained resistant. Loss of resistance to this interferon-sensitive virus correlated with the drop in interferon production.

Finally, we were able to use rats that had been flown in Space Shuttle SL-3. Spleens were removed from these rats and exposed to concanavalin-A [15]. Culture supernatant fluids were harvested and assayed for interferon-gamma and interleukin-3, another immunoregulatory substance. Interferon-gamma production was severely inhibited in flown rats, but interleukin-3 production was normal [15]. This suggests that there may be specific immunosuppressive effects of space flight.

All of these results suggest that further studies are warranted to determine the effects of space flight on immune responses. In addition, studies on the significance of these effects to host health needs to be determined.

PUBLICATIONS

The following are publications relating to this project and acknowledging support of NASA award NCC2-213. Copies of all published articles are appended to this report. Copies of articles in press, submitted and in preparation will be forwarded as a supplement to this report when they are available.

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